

Amendments

In the Claims:

Claim 1 (Withdrawn): A composition comprising a bacterial pilus to which an antigen or antigenic determinant has been attached by a covalent bond.

Claim 2 (Withdrawn): The composition of claim 1, wherein said covalent bond is not a peptide bond.

Claim 3 (Withdrawn): The composition of claim 1, wherein said bacterial pilus is a Type-1 pilus of *Escherichia coli*.

Claim 4 (Withdrawn): The composition of claim 1, wherein pilin subunits of said Type-1 pilus comprises the amino acid sequence shown in SEQ ID NO:146 or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO:146.

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Claim 5 (Withdrawn): The composition of claim 1, wherein said bacterial pilus and said antigen or antigen determinant are attached via a non-naturally occurring attachment.

Claim 6 (Withdrawn): The composition of claim 1, wherein said attachment comprises an organizer comprising at least one first attachment site, and wherein said organizer is connected to said pilus by at least one covalent bond.

Claim 7 (Withdrawn): The composition of claim 6, wherein said organizer is a polypeptide or a residue thereof, and wherein said second attachment site is a polypeptide or a residue thereof.

Claim 8 (Withdrawn): The composition of claim 6, wherein said first and/or a second attachment sites comprise:

- (a) an antigen and an antibody or antibody fragment thereto;
- (b) biotin and avidin;
- (c) strepavidin and biotin;
- (d) a receptor and its ligand;
- (e) a ligand-binding protein and its ligand;
- (f) interacting leucine zipper polypeptides;
- (g) an amino group and a chemical group reactive thereto;
- (h) a carboxyl group and a chemical group reactive thereto;
- (i) a sulfhydryl group and a chemical group reactive thereto; or
- (j) a combination thereof.

Claim 9 (Withdrawn): The composition of claim 1, wherein said bacterial pilus and said antigen or antigenic determinant are attached by an attachment comprising interacting leucine zipper polypeptides.

Claim 10 (Withdrawn): The composition of claim 5, wherein interacting leucine zipper polypeptides are JUN and/or FOS leucine zipper polypeptides.

Claim 11 (Withdrawn): A composition comprising a bacterial pilin polypeptide to which an antigen or antigenic determinant has been attached by a covalent bond.

Claim 12 (Withdrawn): The composition of claim 11, wherein said covalent bond is not a peptide bond.

Claim 13 (Withdrawn): The composition of claim 11, wherein said polypeptide is from a Type-1 pilus of *Escherichia coli*.

Claim 14 (Withdrawn): The composition of claim 11, wherein said bacterial pilin polypeptide comprises the amino acid sequence shown in SEQ ID NO:146 or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO:146.

a | Claim 15 (Withdrawn): The composition of claim 11, wherein said bacterial pilin polypeptide and said antigen or antigenic determinant are attached by a non-naturally occurring attachment.

Claim 16 (Withdrawn): The composition of claim 11, wherein said attachment comprises an organizer comprising at least one first attachment site, and wherein said organizer is connected to said pilus by at least one covalent bond.

Claim 17 (Withdrawn): The composition of claim 16, wherein said organizer is a polypeptide or a residue thereof, and wherein said second attachment site is a polypeptide or a residue thereof.

Claim 18 (Withdrawn): The composition of claim 11, wherein said first and/or a second attachment sites comprise:

- (a) an antigen and an antibody or antibody fragment thereto;
- (b) biotin and avidin;
- (c) strepavidin and biotin;
- (d) a receptor and its ligand;
- (e) a ligand-binding protein and its ligand;
- (f) interacting leucine zipper polypeptides;
- (g) an amino group and a chemical group reactive thereto;
- (h) a carboxyl group and a chemical group reactive thereto;
- (i) a sulfhydryl group and a chemical group reactive thereto; or
- (j) a combination thereof.

Claim 19 (Withdrawn): The composition of claim 15, wherein said attachment comprises interacting leucine zipper polypeptides.

Claim 20 (Withdrawn): The composition of claim 13, wherein said interacting leucine zipper polypeptides are JUN and/or FOS leucine zipper polypeptides.

Claim 21 (Withdrawn): A composition comprising:

- (a) a non-natural molecular scaffold comprising:
 - (i) a core particle selected from the group consisting of:
 - (1) a bacterial pilus or pilin protein; and
 - (2) a recombinant form of a bacterial pilus or pilin protein;and
 - (ii) an organizer comprising at least one first attachment site,
- (b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:
 - (i) an attachment site not naturally occurring with said antigen or antigenic determinant; and
 - (ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said organizer is connected to said core particle by at least one covalent bond; and


wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

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Claim 22 (Withdrawn): The composition of claim 21, wherein said organizer is a polypeptide or residue thereof; and wherein said second attachment site is a polypeptide or residue thereof.

Claim 23 (Withdrawn): The composition of claim 21, wherein said first and/or said second attachment sites comprise:

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- (a) an antigen and an antibody or antibody fragment thereto;
 - (b) biotin and avidin;
 - (c) strepavidin and biotin;
 - (d) a receptor and its ligand;
 - (e) a ligand-binding protein and its ligand;
 - (f) interacting leucine zipper polypeptides;
 - (g) an amino group and a chemical group reactive thereto;
 - (h) a carboxyl group and a chemical group reactive thereto;
 - (i) a sulfhydryl group and a chemical group reactive thereto; or
 - (j) a combination thereof.

Claim 24 (Withdrawn): The composition of claim 21, wherein said first and/or said second attachment sites comprise interacting leucine zipper polypeptides.

Claim 25 (Withdrawn): The composition of claim 21, wherein said bacterial pilus is a Type-1 pilus of *Eschericia coli*.

Claim 26 (Withdrawn): The composition of claim 21, wherein pilus subunits of said type-1 pilus comprise the amino acid sequence of SEQ ID NO:146 or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO:146.

Claim 27 (Withdrawn): The composition of claim 26, wherein said interacting leucine zipper polypeptides are the JUN and/or FOS leucine zipper polypeptides.

Claim 28 (Currently cancelled).

Claim 29 (Currently cancelled).

Claim 30 (Currently cancelled).

Claim 31 (Currently cancelled).

Claim 32 (Withdrawn): The composition of claim 30, wherein said virus-like particle and said antigen or antigenic determinant are attached by an attachment comprising interacting leucine zipper polypeptides.

Claim 33 (Withdrawn): The composition of claim 32, wherein said interacting leucine zipper polypeptides are JUN and/or FOS FOS polypeptides.

Claim 34 (Currently cancelled).

Claim 35 (Currently cancelled).

Claim 36 (Currently cancelled).

Claim 37 (Currently cancelled).

Claim 38 (Currently cancelled).

Claim 39 (Withdrawn): The composition of claim 37, wherein said Hepatitis B virus capsid protein and said antigen or antigenic determinant are attached by an attachment comprising interacting leucine zipper polypeptides.



Claim 40 (Withdrawn): The composition of claim 39, wherein said interacting leucine zipper polypeptides are FOS and/or JUN polypeptides.

Claim 41 (Currently cancelled).

Claim 42 (Currently cancelled).


Claim 43 (Currently cancelled).

Claim 44 (Currently cancelled).

Claims 45 (Withdrawn): The composition of any one of claims 1, 11 and 21, wherein said antigen is selected from the group consisting of:

- (a) an antigen suited to induce an immune response against bacteria;
- (b) an antigen suited to induce an immune response against viruses;
- (c) an antigen suited to induce an immune response against parasites;
- (d) an antigen suited to induce an immune response against cancer cells;
- (e) an antigen suited to induce an immune response in a farm animals;
- (f) an antigen suited to induce an immune response in a pet, and
- (g) any other antigen involved in a pathophysiological context.

Claim 46 (Withdrawn): The composition of claim 45, wherein the antigen is a protein, a polypeptide, or a fragment thereof.

 Claim 47 (Withdrawn): The composition of any one of claims 1, 11 or 21, wherein said antigen is:

- (a) a recombinant protein of HIV;
- (b) a recombinant protein of Influenza virus;
- (c) a recombinant protein of Hepatitis C virus;
- (d) a recombinant protein of Toxoplasma;
- (e) a recombinant protein of Plasmodium falciparum;
- (f) a recombinant protein of Plasmodium vivax;
- (g) a recombinant protein of Plasmodium ovale;
- (h) a recombinant protein of Plasmodium malariae;

- (i) a recombinant protein of breast cancer cells;
- (j) a recombinant protein of kidney cancer cells;
- (k) a recombinant protein of prostate cancer cells;
- (l) a recombinant protein of skin cancer cells;
- (m) a recombinant protein of brain cancer cells;
- (n) a recombinant protein of leukemia cells;
- (o) a recombinant profiling; and
- (p) a recombinant protein of Chlamydia.

Claim 48 (Currently cancelled).

Claim 49 (Currently cancelled).

Claim 50 (Currently cancelled).

Claim 51 (Currently cancelled).

Claim 52 (Currently cancelled).

Claim 53 (Currently cancelled).

Claim 54 (Currently cancelled).

Claim 55 (Currently cancelled).

Claim 56 (Currently cancelled).

Claim 57 (Withdrawn): A method of making the composition of claim 1, comprising combining said pilus and said antigen or antigenic determinant, wherein said pilus and said antigen or antigenic determinant interact to form an antigen array.

Claim 58 (Withdrawn): The method of claim 57, wherein said antigen array is ordered and/or repetitive.

Claim 59 (Withdrawn): A method of making the composition of claim 11, comprising combining said pilin polypeptide and said antigen or antigenic determinant, wherein said pilin polypeptide and said antigen or antigenic determinant interact to form an antigen array.

Claim 60 (Withdrawn): The method of claim 59, wherein said antigen array is ordered and/or repetitive.

Claim 61 (Currently cancelled).

Claim 62 (Currently cancelled).

Claim 63 (Withdrawn): A composition comprising:

- (a) a non-natural molecular scaffold comprising:
 - (i) a core particle selected from the group consisting of:
 - (1) a bacterial pilus; and
 - (2) a recombinant form of a bacterial pilus or pilin protein;and
 - (ii) an organizer comprising at least one first attachment site,
- wherein said organizer is connected to said core particle by at least one covalent bond; and
- (b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:
 - (i) an attachment site not naturally occurring with said antigen or antigenic determinant; and
 - (ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site;

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array, and

wherein said antigen or antigenic determinant is selected from the group consisting of an influenza M2 peptide, the GRA2 polypeptide, the DP178c peptide, the tumor necrosis factor polypeptide, a tumor necrosis factor peptide, the B2 peptide, the D2 peptide, and the A β peptide.

Claim 64 (Withdrawn): The composition of claim 63, wherein said antigen or antigenic determinant is the influenza M2 peptide or variants thereof.

Claim 65 (Withdrawn): The composition of claim 63, wherein said antigen or antigenic determinant is the GRA2 polypeptide.

Claim 66 (Withdrawn): The composition of claim 63, wherein said antigen or antigenic determinant is the DP178c peptide.

Claim 67 (Withdrawn): The composition of claim 63, wherein said antigen or antigenic determinant is the tumor necrosis factor polypeptide.

Claim 68 (Withdrawn): The composition of claim 63, wherein said antigen or antigenic determinant is a tumor necrosis factor peptide.


Claim 69 (Withdrawn): The composition of claim 63, wherein said antigen or antigenic determinant is the B2 peptide.

Claim 70 (Withdrawn): The composition of claim 63, wherein said antigen or antigenic determinant is the D2 peptide.

Claim 71 (Withdrawn): The composition of claim 63, wherein said antigen or antigenic determinant is the A β peptide.

Claim 72 (Withdrawn): The composition of claim 63, wherein said organizer is a polypeptide or residue thereof; and wherein said second attachment site is a polypeptide or residue thereof.

Claim 73 (Withdrawn): The composition of claim 63, wherein said first and/or said second attachment sites comprise:

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- (a) an antigen and an antibody or antibody fragment thereto;
 - (b) biotin and avidin;
 - (c) strepavidin and biotin;
 - (d) a receptor and its ligand;
 - (e) a ligand-binding protein and its ligand;
 - (f) interacting leucine zipper polypeptides;
 - (g) an amino group and a chemical group reactive thereto;
 - (h) a carboxyl group and a chemical group reactive thereto;
 - (i) a sulfhydryl group and a chemical group reactive thereto; or
 - (j) a combination thereof.

Claim 74 (Withdrawn): The composition of claim 63, wherein said first and/or said second attachment sites comprise interacting leucine zipper polypeptides.

Claim 75 (Withdrawn): The composition of claim 63, wherein said bacterial pilus is a Type-1 pilus of *Eschericia coli*.

Claim 76 (Withdrawn): The composition of claim 63, wherein pilus subunits of said type-1 pilus comprise the amino acid sequence of SEQ ID NO:146 or a sequence having at least 65, 70, 75, 80, 85, 90 or 95% sequence identity to SEQ ID NO:146.

Claim 77 (Withdrawn): The composition of claim 63, wherein said interacting leucine zipper polypeptides are the JUN and/or FOS leucine zipper polypeptides.

Claim 78 (Currently cancelled).

Claim 79 (Currently cancelled).

Claim 80 (Currently cancelled).

Claim 81 (Withdrawn): A method of making the composition of claim 63, comprising combining said non-natural molecular scaffold and said antigen or antigenic determinant, wherein said non-natural molecular scaffold and said antigen or antigenic determinant interact to form an antigen array.

Claim 82 (Withdrawn): The method of claim 81, wherein said antigen array is ordered and/or repetitive.

Claim 83 (Currently cancelled).

Claim 84 (Currently cancelled).

Claim 85 (Currently cancelled).

Claim 86 (New). A composition comprising:

- (a) a non-natural molecular scaffold comprising:
 - (i) a virus-like particle that is a dimer or a multimer of a polypeptide comprising, as a core particle, a polypeptide having the amino acid sequence of SEQ ID NO:158, modified such that the cysteine residues at positions 48 and 110 of SEQ ID NO:158 (corresponding to positions 48 and 107 of SEQ ID NO:134) are either deleted or substituted with another amino acid, or a sequence having at least 90% sequence identity to said polypeptide sequence and in which the cysteine residues at positions 48 and 110 of SEQ ID NO:158 are either deleted or substituted with another amino acid; and
 - (ii) an organizer comprising at least one first attachment site, wherein said organizer is connected to said core particle by at least one covalent bond; and

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- (b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:
 - (i) an attachment site not naturally occurring with said antigen or antigenic determinant; and
 - (ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

Claim 87 (New). A composition comprising:

- (b) a non-natural molecular scaffold comprising:
 - (i) a virus-like particle that is a dimer or a multimer of a polypeptide comprising, as a core particle, a polypeptide having the amino acid sequence of SEQ ID NO:134, modified such that the cysteine residues at positions 48 and 107 of SEQ ID NO:134 are either deleted or substituted with another amino acid, or a sequence having at least 90% sequence identity to said polypeptide sequence and in which the cysteine residues at positions 48 and 107 of SEQ ID

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NO:134 are either deleted or substituted with another amino acid; and

- (ii) an organizer comprising at least one first attachment site, wherein said organizer is connected to said core particle by at least one covalent bond; and

- (b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:

- (i) an attachment site not naturally occurring with said antigen or antigenic determinant; and
- (ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

Claim 88 (New). A composition comprising:

- (c) a non-natural molecular scaffold comprising:
 - (i) a virus-like particle that is a dimer or a multimer of a polypeptide comprising, as a core particle, a polypeptide having amino acids 1-149 of SEQ ID NO:134, modified such that the cysteine residues at positions 48 and 107 of SEQ ID

NO:134 are either deleted or substituted with another amino acid, or a sequence having at least 90% sequence identity to said polypeptide sequence and in which the cysteine residues at positions 48 and 107 of SEQ ID NO:134 are either deleted or substituted with another amino acid; and

(ii) an organizer comprising at least one first attachment site, wherein said organizer is connected to said core particle by at least one covalent bond; and

(b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:

(i) an attachment site not naturally occurring with said antigen or antigenic determinant; and

(ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

Claim 89 (New). A composition comprising:

(a) a non-natural molecular scaffold comprising:

- (i) a Hepatitis B virus capsid protein comprising, as a core particle, amino acids 1-149 of SEQ ID NO:134 which is modified so that the amino acids corresponding to positions 79 and 80 are replaced with a peptide having the amino acid sequence of Gly-Gly-Lys-Gly-Gly (SEQ ID NO:158) and in which the cysteine residues at positions 48 and 107 of SEQ ID NO:134 are either deleted or substituted with another amino acid; and
 - (ii) an organizer comprising at least one first attachment site, wherein said organizer is connected to said core particle by at least one covalent bond; and
- (b) an antigen or antigenic determinant with at least one second attachment site, said second attachment site being selected from the group consisting of:
- (i) an attachment site not naturally occurring with said antigen or antigenic determinant; and
 - (ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

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Claim 90 (New). The composition of any one of claims 86-89, wherein said organizer is a polypeptide or residue thereof; and wherein said second attachment site is a polypeptide or residue thereof.

Claim 91 (New). The composition of any one of claims 86-89, wherein said first and/or said second attachment sites comprise:

- (a) an antigen and an antibody or antibody fragment thereto;
- (d) biotin and avidin;
- (e) strepavidin and biotin;
- (f) a receptor and its ligand;
- (g) a ligand-binding protein and its ligand;
- (h) interacting leucine zipper polypeptides;
- (i) an amino group and a chemical group reactive thereto;
- (j) a carboxyl group and a chemical group reactive thereto;
- (k) a sulfhydryl group and a chemical group reactive thereto; or
- (l) a combination thereof.

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Claim 92 (New). The composition of claim 91, wherein said first attachment site is an amino group and said second attachment site is a sulfhydryl group.


Claim 93 (New). The composition of any one of claims 86-89, wherein said antigen or antigenic determinant is selected from the group consisting of:

- (a) an antigen suited to induce an immune response against bacteria;

- (b) an antigen suited to induce an immune response against viruses;
- (c) an antigen suited to induce an immune response against parasites;
- (d) an antigen suited to induce an immune response against cancer cells;
- (e) an antigen suited to induce an immune response against allergens;
- (f) an antigen suited to induce an immune response in a farm animals;
- and
- (g) a protein suited to induce an immune response in a pet.


Claim 94 (New). The composition of claim 93, wherein the antigen or antigenic determinant is a protein, polypeptide, or a fragment thereof.

Claim 95 (New). The composition of claim 93, wherein said antigen or antigenic determinant induces an immune response against one or more allergens.

 Claim 96 (New). The composition of claim 93, wherein said antigen or antigenic determinant is selected from the group consisting of:

- (a) a recombinant protein of HIV;
- (b) a recombinant protein of Influenza virus;
- (c) a recombinant protein of Hepatitis C virus;
- (d) a recombinant protein of Toxoplasma;
- (e) a recombinant protein of Plasmodium falciparum;
- (f) a recombinant protein of Plasmodium vivax;

- (g) a recombinant protein of *Plasmodium ovale*;
- (h) a recombinant protein of *Plasmodium malariae*;
- (i) a recombinant protein of breast cancer cells;
- (j) a recombinant protein of kidney cancer cells;
- (k) a recombinant protein of prostate cancer cells;
- (l) a recombinant protein of skin cancer cells;
- (m) a recombinant protein of brain cancer cells;
- (n) a recombinant protein of leukemia cells;
- (o) a recombinant protein of bee sting allergy;
- (p) a recombinant protein of nut allergy;
- (q) a recombinant protein of food allergies;
- (r) a recombinant protein of asthma; and
- (s) a recombinant protein of *Chlamydia*.



Claim 97 (New). A pharmaceutical composition comprising the composition of any one of claims 86-89, and a pharmaceutically acceptable carrier.

Claim 98 (New). A vaccine composition comprising the composition of any one of claims 86-89.

Claim 99 (New). The vaccine composition of claim 98, further comprising at least one adjuvant.


Claim 100 (New). A method of immunizing, comprising administering to a subject the vaccine composition of claim 98.

Claim 101 (New). The method of claim 100, wherein said administering produces an immune response.

Claim 102 (New). The method of claim 101, wherein said administering produces a humoral immune response.

Claim 103 (New). The method of claim 101, wherein said administering produces a cellular immune response.

Claim 104 (New). The method of claim 101, wherein said administering produces a humoral immune response and a cellular immune response.



Claim 105 (New). The method of claim 101, wherein said administering produces a protective immune response.

Claim 106 (New). A method of making the composition of any one of claims 86-89, comprising combining said non-natural molecular scaffold and said antigen or antigenic determinant, wherein said non-natural molecular scaffold and said antigen or antigenic determinant interact to form an antigen array.

Claim 107 (New). The method of claim 106, wherein said antigen array is ordered and/or repetitive.

Claim 108 (New). A method of immunizing, comprising administering the composition of any one of claims 86-89, or the vaccine composition of claim 98, to a subject, wherein said administering produces a Th2 response that is specific for said antigen or antigenic determinant.

Claim 109 (New). The method of claim 108, wherein antibodies specific for said antigen or antigenic determinant of a subtype corresponding to the Th2 subtype are induced in the subject.

Claim 110 (New). The method of claim 108, wherein the subject does not generate a Th1 response that is specific for said antigen or antigenic determinant.

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